

## OM Forum

# Pandemics/Epidemics – Challenges and Opportunities for Operations Management Research

### ABSTRACT

We have reviewed research papers related to pandemics/epidemics (disease outbreaks of a global/regional scope) published in major operations management, operations research, and management science journals through the end of 2019. We evaluate and categorize these papers. We study research trends, explore research gaps, and provide directions for more efficient and effective research in the future. In addition, our recommendations include the lessons learned from the ongoing pandemic, COVID-19. We discuss papers in the following categories: (a) Warning Signals/Surveillance, (b) Disease Propagation Leading to Pandemic Conditions, (c) Mitigation, (d) Vaccines and Therapeutics Development, (e) Resource Management, (f) Supply Chain Configuration, (g) Decision Support Systems for Managing Pandemics/Epidemics, and (h) Risk Assessment.

**Keywords:** Pandemic; Epidemic; Disease Outbreak; Anthrax; Cholera; COVID-19; HIV/AIDS; Influenza; SARS; Disaster Management.

### 1. Introduction

At the time of writing this paper, the whole world is engulfed in the fury of the COVID-19, a pandemic with its origin in China. Figure A1 in Appendix A shows the growth in the number of pandemic cases worldwide since its outbreak. A brief description of historical pandemics/epidemics, COVID-19 and its growth trajectory, and a description of diseases are included in Appendices A and B respectively. This pandemic has had profound social and economic impacts. Businesses around the globe were closed or had to work below capacity with greatly reduced market demand for extended periods.

Given this grim situation, we set out to review the published literature with the hope of finding some appropriate solutions to the myriad of healthcare, social, economic and political problems that pandemics create. We review, categorize, summarize and synthesize 75 research papers related to pandemics/epidemics. We have used additional references listed in Appendix E to support our arguments and explanations. Then, we critically investigate trends and gaps to provide promising future research directions.

There is no accepted scheme or framework for classifying research on pandemics. In our paper, based on available frameworks (see Appendix C for a review of available frameworks) and the topical coverage in the reviewed literature, we group our findings into the following categories: (a) Warning Signals/Surveillance, (b) Disease Propagation Leading to Pandemic Conditions, (c) Mitigation, (d) Vaccine/Therapeutics Development, (e) Resource Management, (f) Supply Chain (SC) Configuration,

(g) Decision Support Systems for Managing Pandemics/Epidemics, and (h) Risk Assessment. The paper is divided into 11 sections. Figure 1 gives the roadmap for reading this paper. The paper ends with a list of references.

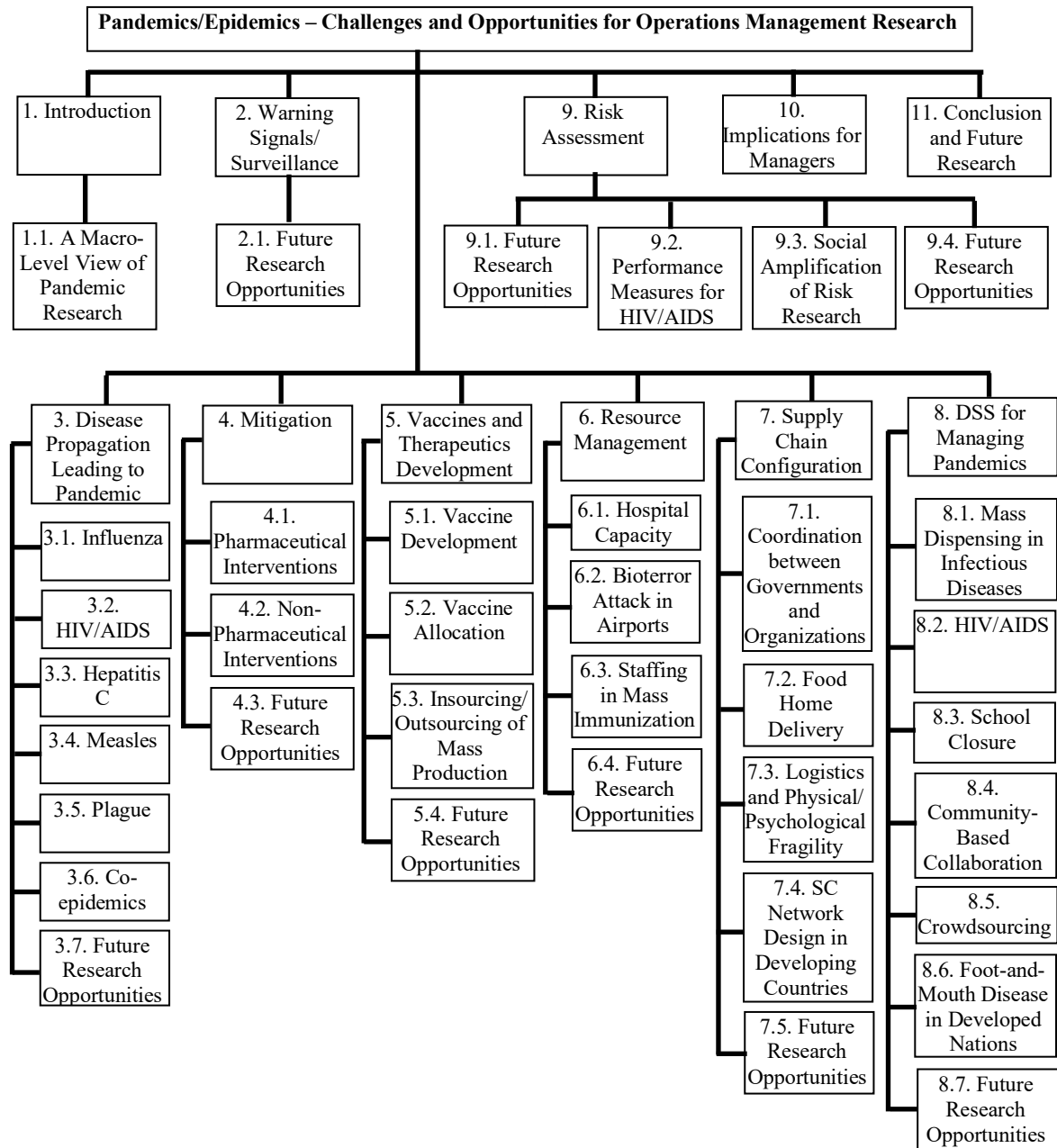


Figure 1: The roadmap for reading this paper.

A macro-level view of pandemic research is given in Appendix D. This appendix includes the methodology we used to search for relevant papers, a chronology of the growth in the number of relevant papers appearing in the pandemic literature, a list of the journals publishing relevant papers, the techniques that these papers used for analyses, and the type of data used by the authors of the relevant papers.

## 2. Warning Signals/ Surveillance

Pandemic surveillance systems are dependent on data sources such as hospital records, sale of pharmaceutical items, social media and news, and methods to identify anomalies that reflect public health issues.

Zhang et al. (2009) and Fast et al. (2018) investigate how social media and online news reports can be used for syndromic surveillance using natural language processing. Zhang et al. (2009) use technical/professional news, whereas Fast et al. (2018) utilize general online news. Zhang et al. (2009) argue that a framework for monitoring and classifying online news for specific diseases will be more effective than a framework for general infectious diseases. To test their suggested framework, they use the major news-based syndromic surveillance systems in the field of infectious diseases such as ProMED-mail, Argus, MiTAP and HealthMap. After the online data acquisition and text document representation, a machine learning algorithm applies feature selection to the text, classifying, condensing and selecting the relevant features.

Fast et al. (2018) study social dysfunction and disruptions (like anxiety, depression, riots, violence, etc.) during disease outbreaks. They utilize real data based on internet articles related to the outbreak of 16 diseases in 72 countries. Then, they apply Bayesian modeling and statistical process control to use the data and predict social response. The results show that the model performance is robust for prediction when there is substantial media coverage (i.e., at least 20 articles per year); but the model's performance is not strong for little media coverage. Some factors that may cause paucity of media coverage include undeveloped online infrastructure, lack of a sufficient number of publication outlets, underestimation of perceived risk, and government censorship. The authors suggest alternative data sources like search engines, social media posts, medical supplies, satellite broadcastings, and meteorological data to increase model accuracy.

Sparks et al. (2010a) and Sparks et al. (2010b) use hospital data to detect warning signals. Sparks et al. (2010a) study a surveillance problem as an early warning tool in the case of natural disease outbreaks or bioterrorism. They monitor data from a group of patients based on the similarity of their syndromes (called syndrome groupings). They call this type of research syndromic surveillance and use various transitional Poisson regression models and time series for forecasting. The parameters used in their models are the amplitude and location of the seasonal peaks, the one-day-ahead forecasts, and forecast errors. They form four syndrome groupings: respiratory, influenza, diarrhea and intestinal infections, and abdominal pain. The researchers observe that the Cumulative Sum (CUSUM) and Exponentially Weighted Moving Average (EWMA) may provide false alarms in the presence of non-normality. Further, EWMA may not perform well for Poisson counts with low mean values. They monitor amplitude and seasonal peaks' location and investigate errors for two models: adaptations of CUSUM and EWMA. Their research shows that adaptive EWMA is superior to CUSUM. Similar to Sparks et al. (2010a), Sparks et al. (2010b) study a surveillance system but the focus is on different diseases. Their suggested model accommodates patients' behavioral data in recent past years over public holidays, school holidays, weekdays, and weekends. They apply classic control chart methods.

The main difference between this and prior research is that they do not consider standardized forecast errors and the assumption of normality. Accordingly, they propose an adaptive EWMA model which is effective for early detection by epidemiologists.

Frisén (2014) adds time and location aspects and studies spatial outbreak detection methods for surveillance. The author studies four different locations and time of event scenarios using regression-based techniques for multivariate surveillance: (i) detection of outbreaks in clusters that have increased incidences in geographically close regions; (ii) detection of an outbreak in an unknown location among many locations; (iii) simultaneous change (i.e., increase) of outbreaks at all locations; and (iv) outbreaks in different regions with time lags. To validate the methods, two evaluation metrics are used: false alarms and detection delay. The methods are tested for data related to seasonal influenza in Sweden.

The above research studies do not consider uncertainty which is an important topic for future research in studying surveillance systems. Gailis et al. (2014) investigate how uncertainty in an epidemic's early stages can be estimated. They propose a scenario-based tree to observe various possible paths that can be taken by an epidemic and syndromic signals. For the epidemic part, a stochastic SIR (susceptible, infected, recovered) model is utilized to consider the underlying social network and its connectivity. For the syndromic signals (e.g., absenteeism or rising sales for some pharmaceuticals items), beta distributions are considered that lag the epidemic. The authors generate time series for the epidemic and syndromic signals through simulation and feed these results to the scenario trees. Using data from the literature, the suggested method is validated based on accuracy in forecasting future outcomes. The authors show that the syndromic signals can provide a reliable early warning if the infected and non-infected people can be properly distinguished.

## **2.1. Future Research Opportunities**

The research for early detection of an outbreak study both specific and general diseases based on either special-purpose data (e.g., health news and hospital data) or general-purpose data (e.g., internet-based data). However, online data are not always derived by experts and analysts of healthcare systems. The dominant technique to analyze data is statistical analysis. Besides, scenario-based techniques (i.e., simulation and decision analysis), learning techniques (i.e., Bayesian network and machine learning) are also used.

Research about the detection of new diseases – which is currently peripheral to health professionals – can be useful in terms of symptoms. There is a great creative opportunity in this domain. A network of doctors could be established to provide constant monitoring of healthcare status on a global basis as well as evaluations of the state of the systems. Observe unexpected spikes in absenteeism and spikes in demand for generic drugs which are pain killers, etc. Drug companies could provide valuable information time series data about generic drugs. Other observations could be provided by those who are involved in such systems in a variety of different ways. Detection and

surveillance problems deal with a large amount of data and a high level of uncertainty for which big data analytics, machine learning, and other learning-based models present attractive opportunities. This provides the chance to emphasize uncertainty applied to the study of surveillance systems.

### **3. Disease Propagation Leading to Pandemic Conditions**

There is an elapsed time between the exposure to a pathogen and the appearance of the symptoms which is called the incubation period. The longer the incubation period, the more dangerous the situation becomes. Read Appendix B for a description of incubation period and reproduction/reproductive rate/ratio/number for various diseases.

Kermack and McKendrick (1927) introduced the well-known compartmental model SIR in the field of epidemiology. In this model, a large population is split into three compartments: S (Susceptible), I (Infectious) and R (Recovered). An individual belongs to only one of these compartments and may move from one compartment to another. A system of differential equations is formed to show the flow between compartments at any time. Later, the SIR model was extended to SEIR, MSEIR, MSEIRS, SEIRS, SIR, SIRS, SEI, SEIS, SI, and SIS models depending on application for various diseases (Herbert and Hethcote, 2000). In these models, E represents the exposed compartment, and the M compartment stands for the passively immune class, such as infants with passive immunity. Gani (1987) extends and generalizes the two models developed by Kermack and McKendrick (1927) and Whittle (1955) based on the concept of a bunching model, which is attributed to Saunders (1980). The existing models may miscalculate disease outbreak if there is a bunching behavior where people collect in compact groups.

#### **3.1. Influenza**

Larson (2007) and Teytelman and Larson (2012) develop discrete-time models to study influenza pandemic progression. Larson (2007) focuses on the heterogeneity of the population. The behavior of a population, being socially active or inactive, can significantly affect disease propagation. This paper also studies “social distancing” as a behavioral control mechanism. Social distancing refers to the frequency and closeness of human-to-human contact and also includes quarantining. The author divides susceptible populations in terms of frequency of contacts and their infection propensity to show the disease’s evolution over time. Three models are analyzed: (i) active and inactive people, (ii) contacts over time, and (iii) social distancing and hygienic factors. The author uses a numerical example with existing data from nine countries. The research shows that social distancing can significantly control the outbreak as a non-pharmaceutical solution. If it is implemented effectively, it can even eradicate the disease.

Teytelman and Larson (2012) generalize the model proposed by Larson (2007) by considering a continuous form of population heterogeneity, but time is still discrete. In their research, population heterogeneity means people are different from each other in terms of social activity and proneness to

infection, shedding virus and spreading infection. The research shows that the distribution of contact rates is highly important. In the initial periods of the outbreak, active people become infected and immune. Over time, inactive/low active people will dominate among susceptibles.

### **3.2. HIV/AIDS**

Kaplan (1989) investigates the transmission of AIDS among gay men. The author models epidemic spread considering the incubation period of HIV and the duration of sex lives, which is the time a man enters an uninfected sexually active population until he leaves it. Following Kaplan (1989), Kaplan and Brookmeyer (1999) suggest a new method for estimating HIV incidence. In this research, a marker (that includes cellular concentration and immune-activation) shows time from infection available in the body of a person (named CD4) to estimate history and progression. The count of CD4 via sampling at a point in time provides information about the infection in a population. The researchers suggest using a Markov model based on the marker. Such a method can be used in a prevention program and particularly for resource allocation. The authors state that their method is easy to implement, but the drawback is that it is still lagged into the past and may be biased for new infections.

Griffiths et al. (2000) divide population under study into three subgroups: susceptible to infection, infected with HIV, and those who have developed AIDS. They draw flow diagrams to show how the disease is transmitted among different sub-populations within different age groups. The authors develop a system of differential equations and parametrically solve it. The research shows that the intervention policies, promotion of safe sex and the evaluation of cost savings by providing treatment, should target younger age groups (particularly those under 35). It means investing in older age groups is not worthwhile in terms of reducing the number of cases.

Griffiths et al. (2006) extend the work of Griffiths et al. (2000). The authors observe that traditional models like SIR and SIS are not appropriate for HIV/AIDS because individuals cannot recover from this disease; only treatments and therapies can help affected people live longer. Therefore, they design an extended version of SI. Their model considers the following five sub-populations at any time; the numbers of susceptibles, high-risk infectives, low-risk infectives, high-risk AIDS cases, and low-risk AIDS cases. The authors use “difference equations” and solve the model. Depending on the types of treatments applied to people in different stages and times, and the natural history of HIV infection, the effect of drugs can be estimated. Using a maximum likelihood estimation procedure, the authors show that the model can be used to estimate future incidence/prevalence levels. The researchers test their model based on data related to the homosexual population in the UK and show its practicality and extrapolate the trajectory of the five variables. The results identify preventive measures to be applied to a population in the future.

Roberts and Dangerfield (1990) and Xuan et al. (2009) use systems dynamics to examine the HIV/AIDS epidemic. Roberts and Dangerfield (1990) divide the homosexual population into

susceptible, HIV-infected, under treatment, clinical population and deaths. The model captures the incubation period and virological and behavioral features among these people. The authors draw an influence diagram for the disease transmission and solve their model using a system dynamics simulation software. They validate the model using UK data. Xuan et al. (2009) consider four groups whose behaviors are different in terms of infectivity, susceptibility, mobility and degrees of influence on others. The research considers the realistic state of an individual: healthy, dangerous, infected (but not infectious), infectious (but not asymptomatic), symptomatic, and deceased. The authors develop CA (cellular automata) simulation model to analyze the problem. Their research findings show that an HIV/AIDS epidemic can end up with either extinction or persistence. Factors such as population density, initial infection rate and mobility identify that the final result will be extinction or persistence. Moreover, while people who have very high infective susceptibility are few, they massively affect the infection rate and the outcome. Extensive documentation of the applications of systems dynamics to study AIDS can be found in a survey paper by Dangerfield (1999).

### **3.3. Hepatitis C**

Hepatitis C can be transmitted in different ways such as unprotected sex, blood donation, tattooing, body piercing, mother to child and needle-stick. Mather (2000) simulates the spread of blood-borne diseases with a special focus on hepatitis C to evaluate the effects of interactions, immunizations, and treatment factors. The author considers a closed cohort of injecting drug users with three subgroups: susceptibles, infectives and immune. The researcher uses a Markov model and studies the progression of the disease. The research shows that only with a low interaction level and low probability of infection can a high prevalence level be prevented. The author believes that the proposed model can provide what-if analysis to investigate the impact of changes in parameters such as transition probabilities, disease prevalence within groups, the average number of contacts per week, probable immunization, treatment factors, and minimum duration in each state.

### **3.4. Measles**

Yakowitz et al. (1992) investigate the application of automatic learning as a stochastic optimization algorithm that converges through repetition in epidemics. The research considers Markov states based on the SIR model for a general contagious disease. The SIR model divides people into susceptible, infected and removed (dead or immunized) at any point in time. As the epidemic develops over time, the population is partially immunized which reflects a learning process. This technique has been in use for measles, gypsy moth and crabgrass diseases (Durrett, 1988). The authors describe the applicability of the technique for spatial epidemic control. They study the immunization problem to show learning methods are applicable to epidemics. Accordingly, they compute the associated Markov probabilities. To do that, they apply the concept of dynamic Markov modeling - a variation of Markov sequencing- to describe spatial models for a contagious disease. The Markov model considers

the state of the people as susceptible and infected that changes over time.

### **3.5. Plague**

Carvalho-Rodrigues et al. (1993) explain epidemics based on the concept of entropy in thermodynamics. The concept of entropy has already been applied to complex systems like societal structures. Following the concept of the Shannon entropy model (Shannon, 1948a, 1948b), they see the concept as a predictor for the collapse of social cohesion when facing a disaster due to a disease outbreak. Empirical data was available about Lisbon's plague for different periods from the 14th century to the 17th century. The authors consider the data for different zones of the city. For example, in seaports, more people are infected than in rural villages. The analyses on the existing data in terms of the numbers of casualties and combatants in different zones are conducted in different time periods (over several centuries). The research shows that if the mortality rate reaches around 37%, societal collapse happens. Collapse means the affected area goes into decline and is unlikely to be urbanized.

### **3.6. Co-epidemics of HIV and Tuberculosis**

Long et al. (2008) study a co-epidemic problem, which means the spread of one contagious disease causes the spread of another one. An example of co-epidemic is the spread of HIV that can stimulate the spread of tuberculosis (TB). The authors develop two models for this problem. In the first model, they split people into susceptible and infected. In the second model, for the first disease, people are divided into susceptible, infected with no symptom, and infected with symptoms; for the second disease, people are divided into susceptible, exposed, and infected. The main decisions are whether to treat HIV or TB individually. Alternatively, coordinated treatment can be applied. The authors formulate the problem using a system of nonlinear differential equations and solve them analytically. The following equilibria have been defined and derived: disease-free equilibrium, quasi disease-free equilibria, and co-infection equilibrium. The research findings show that treatment efforts on a targeted epidemic may mitigate it but can worsen spread of the other. The authors recommend a coordinated effort in which both epidemics are treated. However, the researchers believe treatment by itself is not enough for the eradication of the diseases. Accordingly, coordinated prevention efforts are required.

The final recommendation by Long et al. (2008) (i.e., treatment) is followed by Lebcir et al. (2010) who study HIV/AIDS, TB, and multidrug-resistant tuberculosis (MDRTB). These diseases and their treatments are interdependent. WHO has suggested using highly active antiretroviral therapy (HAART) for HIV/AIDS and some other drugs (named second-line drugs) for MDRTB for concurrent treatment. The research investigates HAART and MDRTB coverage levels considering their treatment rate and HIV and TB transmission dynamics. The authors draw a causal diagram based on the transmissions between TB, MDRTB and HIV to apply a system dynamics simulation model and analyze various scenarios. The model is tested on data from Russia and shows that the



relationship between HAAR coverage and the number of deaths is not linear. If HAART coverage is less than 50%, its impact is not significant in reducing deaths from TB and HIV-associated TB. It is recommended the coverage to be above 70% to ensure significant impact.

### **3.7. Future Research Opportunities**

We find that research on propagation, leading to pandemic conditions, is focused on diseases HIV/AIDS, influenza, tuberculosis, Hepatitis C and foot-and-mouth disease. Some recent studies have focused on co-epidemics that relate co-existence of two diseases. Various concepts like thermodynamics, automatic learning and rumor control have been used to model disease transmission. The existing research widely uses F&A data and it is reasonable to assume its continuity in the future due to data availability. At the same time, new developments in data mining and AI's reliance on copious amounts of data provide exciting future research opportunities.

In the future, research will continue to be virus-specific as the nature of the disease and its transmission behavior significantly affect modeling. Therefore, before modeling, broad-based knowledge of the studied virus is required. Another observation is that compartmental models are the backbone of pandemic modeling which applies to oversized and populous areas, but they may not be precise for small areas such as within hospitals which provides another research opportunity. Further, advancements in technology can enable researchers to develop efficient systems to support predictions about the control of disease propagation as well as other decisions.

Systems dynamics may provide opportunities to expand the number of relevant variables, including behavioral factors, which are often crucial in determining the spread rate. In fact, human behavior is not widely understood and may play a greater role in efforts to control epidemic and pandemic levels. Human behavior is an important factor in the spread of coronavirus. So, it may not be that new models are required but rather that existing models be expanded to include variables that are considered difficult to quantify.

## **4. Mitigation**

Mitigation refers to the pharmaceutical and non-pharmaceutical interventions that minimize the spread of disease. Pharmaceutical interventions include vaccinations, medicines and treatments, whereas non-pharmaceutical interventions include quarantine, isolation, social distancing, travel restrictions, numerical limits on public gatherings, school and business closings.

We discuss two survey papers, Jaquette (1972) and Wein et al. (2009) that deal with mitigation issues. Jaquette (1972) reviews mathematical and quantitative decision theory models for epidemics. The paper shows that control theory, Markov decision processes and simulation, with deterministic/stochastic and continuous/discrete times have been used in epidemiology. However, the paper's major contribution is introducing applications that are not limited to disease outbreaks. Wein et al. (2009) highlight research on preparing for and responding to bioterror through three potential

attacks, namely anthrax spread, attacks on food supply, and pandemic influenza.

#### 4.1. Pharmaceutical Interventions

Vaccines are pharmaceutical products that provide full or partial immunity to a specific disease by reducing transmission and mitigating outbreaks for a significant percent of the population. Vaccination programs have been the most effective approach to preventing widespread infectious diseases (CDC, 2011). To see various types of vaccines, review Callaway (2020).

We have discussed below the cost-effectiveness of various mitigation alternatives, the enforcement decisions, and the importance of personal decisions.

##### 4.1.1. Cost-Effectiveness

**Methods for general diseases:** Sethi and Staats (1978) find the optimal policy for vaccination levels. The state variables are the numbers of infected and susceptible people; the control variables are the levels of medicare and inoculation program efforts. Three mathematical models are suggested.

Like Sethi and Staats (1978), Lefevre (1981) studies a contagious disease in a finite population divided into infectives and susceptibles. The disease can be transmitted from infectives to susceptibles. Some infected people recover. Using a discrete-time Markov chain, the authors model the problem as a birth-death process and solve it analytically. The objective function is the minimization of discounted cost over an infinite time horizon. The cost function is the summation of the social cost (based on the number of infectives) and control cost (per unit time adopting quarantine). The researcher shows that this problem is similar to a rumor control problem where an external source (e.g., newspapers and television) acts similar to an infection process.

Piunovskiy (2004) considers the number of susceptible people and disease carriers as the state variables at a point in time. The jump from one state to another is not controllable. The problem is modeled as a continuous-time-jump Markov process and formulated as a dynamic programming problem. There are two performance criteria: the total (expected) number of susceptibles who have been infected and the total (expected) number of susceptibles who are immunized. Both criteria are to be minimized in the Bellman dynamic programming equation to find the optimal intervention strategy.

**Methods for specific diseases:** Zaric et al. (2000) investigate the cost-effectiveness of methadone, a drug used in heroin addiction treatment. The researchers divide the population into three categories: uninfected, HIV infected without AIDS, and infected with AIDS. They also consider three risk groups for injection drug users (IDUs): IDUs who are not in treatment, IDUs who are in treatment, and non-IDUs (who do not inject). These two categorizations make nine compartments of the population. Infection can be transmitted in two ways: sexual contacts and drug injection. Healthcare and medication costs/benefits measured in terms of quantity and quality of life are analyzed. The authors explore the transition rate among the nine different compartments and form an associated system of differential equations. The researchers use real data from various sources and solve the model. Their

research shows that the methadone program is cost-effective, even in groups with low HIV incidents. Additionally, the greatest cost savings in the healthcare system have occurred because of HIV care cost-saving.

Whereas Zaric et al. (2000) implicitly consider that there are sufficient vaccines available for the whole population, Kress (2006) considers the possibility of limited vaccine supply and, therefore, the need for an inevitable prioritization. Kress (2006) considers a bioterror attack with a contagious virus (here, smallpox) that can cause an epidemic. The research investigates response policies against such an event as epidemic-intervention: (i) mass vaccination that uses the overall capacity to cover the whole population, (ii) trace vaccination (also called ring or targeted) that uses a limited vaccination capacity and applies to infected (or suspected) people, and (iii) *prioritized vaccination process (PVP)*. In PVP, the trace queue has priority; then, additional vaccination capacity is used for the general mass queue. This virus has an incubation period and will be asymptomatic for a while. The author assumes that infected people are not infectious during the incubation period and divides the incubation period into two smaller periods as immunable and non-immunable. During the immunable period, which is also called vaccine sensitive, vaccine is effective and there is a high chance to eliminate the disease from an infected person. During the non-immunable period, vaccine cannot eliminate the disease and the infected person will be ill in the end. After the incubation period, the individual will be infected with symptoms. Effectiveness, based on the maximum tracing probability, shows that the most effective policy is PVP (see iii above).

#### **4.1.2. Implementation Issues**

***Swine influenza vaccination:*** Zalkind and Shachtman (1983) suggest a decision tree analysis to estimate the non-economic value of life/death. The authors use the term “non-economic value of life/death” as a surrogate for the probability of death. Their suggested method works based on the decisions made by individuals. A person decides whether to receive the vaccine considering its positive and negative consequences. The data related to the values, probabilities and consequences regarding the reaction to a flu jab, contracting swine influenza, dying from swine flu, the chance of swine flu occurrence and vaccine efficacy are included in the decision making process. The research uses lottery construction in modeling and analysis. The authors believe that a decision tree is an appropriate tool for determining the non-economic personal value of life in a situation like epidemics when dealing with an individual’s decision. An adverse event may(not) happen. An individual may(not) accept vaccination. In either case, there can be positive and negative aspects.

***Hepatitis C:*** Behrens et al. (2008) study the spread of the hepatitis C virus (HCV). From among its various transmission modes, the research focus on contaminated tattoo equipment. Sterilization of equipment can solve the issue but it incurs an additional cost of around 15% per tattoo, causing resistance from businesses. The research investigates possible interventions to be examined by the government as regulations. The authors formulate the spread problem in a dynamic setting and

include the number of sterilizations and HCV infections over time. By using real data, the authors conduct sensitivity analyses. Their findings show that intervention via regulating and enforcing tattoo parlors is cost-effective for HCV control.

***Treatment prioritization for hepatitis C:*** Ayer et al. (2019) investigate how prisoners suffering from hepatitis C virus (HCV) infection need to be prioritized for treatments. The appropriateness of prioritization is identified based on criteria such as liver disease and remaining sentence length (short or long). The objective function is to minimize the quality-adjusted life years (QALY) that considers both (i) reduction in an infected patient's life expectancy/quality and (ii) potential value loss from future transmissions. The authors model the problem mathematically and solve it by using agent-based simulation. The common practice is prioritization based on only liver health status. The research shows that unlike current practice, remaining prison sentence length and IDU status should also be considered with the liver health status.

## **4.2. Non-Pharmaceutical Interventions**

Non-pharmaceutical interventions focus on social distancing to reduce contact among people. They also include masks, hand-washing, hand-sanitizers, contact tracing, etc. Research opportunities about the effectiveness of various strategies for each of these categories are blatantly evident. For example, most masks that people wear are in no way related to the standards of the N-95. What effect does the constant touching by people of their individual masks have in diminishing the benefit of masks? We could go on in the same vein with respect to hand-sanitizers and bogus marketing, contact tracing and the refusal of many to cooperate,

### ***4.2.1. Quarantine and Isolation***

***Quarantine for a general disease:*** Sethi (1978) divides populations into susceptibles and infectives and formulates a quarantine problem to be used as a lever by authorities to control a disease outbreak. The model contains a control variable that continuously changes between 0 and 1 to adjust the contact rate between people. The author formulates the problem with a linear social cost function for an infinite horizon and solves the problem analytically using a mathematical model with differential equations. Eventually, the model is extended for a finite horizon application (e.g., seasonal influenza).

***Isolation for Ebola:*** Büyüktaktın et al. (2018) study the spatial spread of infectious diseases between susceptible, infected, treated, recovered, and dead people. The model dynamically determines when and how much of the existing resources need to be assigned to various locations. The model minimizes the sum of infected people and fatalities subject to budget and capacity limitations. The research shows that immediate isolation (i.e., reducing contact rate), improving recovery rates, precautions in funeral and burials, and education significantly affect the number of infected people and fatalities.

#### **4.2.2. Travel Restrictions**

**Travel restriction for influenza:** Nigmatulina and Larson (2009) follow Larson (2007) to study how to mitigate the spread of pandemic influenza. This research adds travel restriction to the previously studied strategies (i.e., social distancing and hygiene) to investigate the impact of interventions to stop virus spread. Moreover, it considers several heterogeneous communities that are loosely linked. They develop a mathematical model for their multi-community problem to observe spatial spread. The research indicates that non-pharmaceutical intervention can make a significant difference even if vaccination is not used. The authors do not recommend that governments enforce travel restrictions but suggest advance travel advisories before an outbreak to urge voluntary travel reduction.

#### **4.2.3. Adherence**

Adherence, a term linked to behavioral psychology in healthcare, is defined as “the extent to which a person’s behavior, taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider” (Chakrabarti, 2014). Similarly, McCoy et al. (2014) define a patient’s adherence as his/her willingness and commitment to a treatment program. They consider adherence and the growth of epidemic diseases simultaneously in a capacity planning problem to investigate the effectiveness of treatment. This research assumes that people who are geographically close to their health providing facilities maintain a higher level of adherence. Patients are heterogeneous and may not have the same commitment to adherence for various reasons. For example, patients who live in rural areas, far from their health facilities, may have less adherence. The researchers suggest a nonlinear mathematical model that determines the number of patients to be enrolled in a specific clinic. The objective function minimizes the average of the infected population in future periods subject to a budget limit. The model is analytically solved. The authors use real data related to HIV of rural Zambia and show that ignoring adherence and health delivery can significantly overestimate the effectiveness of a treatment program.

#### **4.2.4. Hybrid Interventions**

**Mixed strategies for influenza pandemics:** Das et al. (2008) design a simulation model for controlling influenza outbreaks. The model considers the stochastic spread of the disease and shows the impact of a pandemic based on measures such as the number of infectives, deaths, people denied hospital admission, denied vaccines, and total cost, including healthcare costs and wages. Various mitigation strategies can be applied to the model to observe the impact of vaccination, prophylaxis, hospitalization, social distancing, and voluntary and mandatory quarantine. The model is tested by using hypothetical data. The authors suggest a framework that works based on a Markov decision model and its simulation-based learning.

***Pharmaceutical and non-pharmaceutical strategies for H5N1:*** Uribe-Sánchez et al. (2011) investigate a resource utilization problem considering societal and economic dynamics. They study dynamic and predictive mitigation strategies for a pandemic outbreak and develop an optimization model to determine mitigation strategies for health policy makers. The possible mitigation strategies are pharmaceutical (e.g., vaccine and antiviral) and non-pharmaceutical (e.g., social distancing). The objective of the model is to minimize the costs of lost productivity and medical expenses. These cost items are linked to morbidity, mortality, and social distancing. They formulate the problem based on the SEIR model and solve it by a simulation-optimization algorithm. The research findings show that (1) vaccine efficacy for low transmissibility scenarios is not significant compared to high transmissibility scenarios; (2) social distancing conformance significantly affects the pandemic cost, particularly for higher transmissibility scenarios; (3) early declaration of social distancing will significantly decrease the number of infected people and deaths.

Ventresca and Aleman (2014) investigate the containment phase of disease spread applied to vaccination, quarantine or isolation. The problem is to choose a subset of nodes in a network exposed to a contagious disease so that the number of affected nodes is less than a given number. It is assumed that the disease affects the population, starting with a single individual. Each node in the graph has a population size that determines the probability of an outbreak in that node. If a node contains an infected individual, then all people in that node are likely to be infected. The authors formulate the problem as an integer programming model to minimize the number of nodes to be removed. The authors suggest a local search algorithm to find near-optimal solutions. The researchers validate the algorithm against four benchmark models, namely Erdős–Renyi, Barabasi–Albert, Watts–Strogatz small world, and forest fire (Leskovec et al. 2005).

#### **4.3. Future Research Opportunities**

Mitigation of pandemics/epidemics, using simulation and stochastic modeling, has been a popular research area over the last two decades. The intervention strategies for mitigation are divided into pharmaceutical, non-pharmaceutical, and hybrid. In pharmaceutical interventions, cost-effectiveness, enforcement and individual decisions have been investigated for general and specific diseases. When it comes to non-pharmaceutical interventions, quarantine, isolation, travel restriction, and adherence are studied. Finally, few research papers have considered a mixture of pharmaceutical and non-pharmaceutical interventions. A critical gap in the research is the lack of focus on research in healthcare supply chains (SCs) where hospitals and emergency departments are involved. Also, there are very attractive modeling concepts that can be pursued such as the rumor control problem where external sources such as tweets and Facebook messages can be studied as analogs to disease infection processes.

The research on pharmaceutical intervention is effective if they focus on the specific disease rather than general. The current research focuses on swine influenza and hepatitis C. Therefore, it can

be extended to many other unexplored diseases. In particular, we recommend researchers to consider COVID-19. The research on non-pharmaceutical intervention is also either on general disease or specific ones like Ebola and influenza. However, the existing non-pharmaceutical approaches are commonly effective for most contagious diseases. In case of COVID-19, we observe that some nations enforce such guidelines and some others recommend it. It is an important research direction so see under what conditions these approaches should be applied voluntarily or enforced.

## **5. Vaccines and Therapeutics Development**

Developing an effective vaccine for a new disease is a complicated, costly, and time-consuming challenge (Oyston and Robinson, 2012). After identifying the virus strain, vaccine development requires testing, bulk manufacturing, quality control, batch filling and distribution, and release. In case of new viruses, major uncertainties are identifying, preparing, and verifying the vaccine strains (WHO, 2009).

### **5.1. Vaccine Development**

Wu et al. (2005) investigate a vaccine strain selection problem focusing on influenza viruses. Annual influenza vaccines are based on the virus' historical evolution because influenza evolves in a random sequence of mutations (so-called *antigenic drift*). How to formulate and develop vaccine-strains is computationally complex because it is a high-dimensional, multi-period, stochastic process. All potential vaccines are mapped with respect to efficacy and safety against each identified viral type of the epidemic. Dynamic programming is then used to find a near-optimal, closed-form approximation for a single-period version of the problem. Research shows how such a multi-period complex problem can be tackled by solving a series of single period problems.

### **5.2. Vaccine Allocation**

#### **5.2.1. Timing in vaccination**

Yarmand et al. (2014) consider a vaccine allocation problem for an infectious disease like influenza in two phases. In phase one, vaccine doses are allocated to regions with the objectives of cost minimization and containing the outbreak. In phase two, additional doses of vaccine are allocated with the same objective but for regions in which the epidemic is not contained. The authors simulate the problem as a two-stage stochastic formulation which they convert to a linear model; develop a newsvendor equivalent of the problem, and suggest a heuristic algorithm. Their research shows that epidemic alerting and detection is valuable only if vaccination coverage in phase one is low.

Similar to Yarmand et al. (2014), Duijzer et al. (2018a) also study timing in vaccination but focus on changes in vaccine type rather than using the same vaccine in different phases. The authors study timing for choosing between a specific or an aspecific vaccination. Aspecific vaccines are available before pandemic influenza but may not be efficient for upcoming influenza as the viruses can evolve.

Specific vaccines are those that are designed and produced after a known pandemic happens. Aspecific vaccination may prevent a large outbreak, but specific vaccination has an advantage as it is tailor-made and more effective. Therefore, specific vaccines are efficient but will be available late when many people are affected. There are two approaches to avoid an outbreak: (i) aspecific vaccinations in the early stages with limited information on the disease, and (ii) specific vaccination later. Using the SIR model, the authors formulate the problem mathematically to calculate the fraction of people who are not susceptible and immune. The objective function is the minimization of the infected proportion of the population. Trade-offs between timing, efficacy and controlling the epidemic show that an optimal strategy is not to spend the budget on a single strategy; a hybrid strategy that contains both approaches is best. Based on the data in the literature related to H1N5, the findings show that vaccinating a fraction of the population at the early stages (with aspecific vaccine) and, after a while, switching to the specific vaccine can reduce infection rates by at least 50%.

### ***5.2.2. Geographically different regions/ populations***

While Duijzer et al. (2018a) investigate the vaccination problem in terms of timing, Duijzer et al. (2018b) focus on multiple, non-interacting populations. They highlight two ways to achieve immunity: vaccination (direct effect) and herd immunity (herd effect). Herd immunity refers to the scenario when a sufficiently large number of people in a community are immune to a disease (by vaccination or by recovering from the diseases that often bestow immunity. In such cases, the community is immune as propagation of the disease through individuals is unlikely (MFMER, 2020). This research investigates which population groups should be under direct effect and which groups should be under herd effect when there is a limited vaccine stockpile. The objective is to maximize the number of people who escape infection. Based on the SIR model and SEIR (an extension of SIR), the authors formulate the problem mathematically to decide what fraction of the population needs to be vaccinated. The research shows that allocating the limited vaccine stockpiles based on multiple doses for some populations is more effective than equally using a single dose to all people. However, they believe that this approach can be criticized on ethical grounds.

### **5.3. Insourcing/Outsourcing of Mass Production**

Adbi et al. (2019) empirically investigate pandemics in emerging economies, focusing on the H1N1 influenza vaccine in India. They state that in India, vaccines are supplied through either domestic or multinational organizations. The main research question is how domestic and multinational organizations should respond to a shocked demand caused by a pandemic in a developing country. Further, they study how targeted policies - such as advance commitments/contracts for the response phase, and providing incentives for domestic suppliers/ manufacturers to develop new vaccines and therapeutics - can help in such pandemics. By using vaccine purchasing data from India during the 2009–10 global H1N1 pandemic, the authors show that there will be a huge shift toward domestic,



newly developed vaccines and therapeutics in the case of a pandemic. Sufficient incentives need to be provided for domestic manufacturers. This arrangement is preferred to advance contracts with multinational suppliers.

#### **5.4. Future Research Opportunities**

Vaccine development continues to be in the domain of researchers in pharmaceutical companies. This area remains unexplored by the OM community. However, it can benefit from OM research in the “new product development” field. Unlike profit motivations in commercial markets, incentives can include humanitarian considerations that are wielded by society as well as governmental agencies. The OM community can also contribute to the development of superior logistics of vaccine distribution.

There are research potentials for unknown viruses that evolve over time requiring new specific vaccines. Designing and producing new vaccines takes a long but uncertain time. On the other hand, there are always some medicines and vaccines available before a pandemic. Using these specific vaccines may save time, cost, and lives if they mitigate the impact of a sudden pandemic. Investigating the nature of viruses, (dis)advantages of the early specific vaccination, the timing and target population to be vaccinated as a quick mitigation approach can be important topics for future research. The focus of this paper is on vaccines and therapeutics for pandemics/epidemics. In that regard, readers interested in influenza can refer to Keskinocak and Savva (2020), Deo and Corbett (2009) and Cho (2010) that focus on influenza.

### **6. Resource Management**

#### **6.1. Hospital Capacity**

Sun et al. (2014) study collaboration between several hospitals to allocate patients in the case of an influenza pandemic. The model has two objective functions: minimization of patients’ (i) total travel distance and (ii) the maximum travel distance to hospitals. The decision to be made is to allocate patients to hospitals. The constraints are the availability of critical personnel and vital equipment. The problem is formulated as three linear models: a single period model considering objective function (i); a bi-objective multi-period model by adding objective (ii) as a proxy for equity between patients; and a bi-objective model by adding hospital resource limitation constraints to the second model. The authors use the constraint method to convert models with two objectives to a single objective model.

Sun et al. (2014) study patient allocation without considering implementation aspects. Liu and Zhang (2016) suggest four phases comprising forecasting, planning, execution, and adjusted forecasting (FPEA) that work continuously as a closed-loop. They implement these phases and apply them to medical resource allocation in epidemics. The forecasting phase works based on the SEIR model. In the planning phase, a multi-period, mixed-integer model decides whether or not each hospital has the capacity to be operational in each period to minimize the operations and logistics

costs for supplying, distributing and allocating hospital beds. Moreover, a quadratic programming model is used for the execution phase. The model is adjusted periodically to minimize errors. The four-phase loop is tested on hypothetical data.

In contrast to the above research, Long et al. (2018) design a two-stage model to consider the heterogeneous geographic spread of epidemics. In the first stage, they utilize historical data related to 21 regions of the 2014 Ebola epidemic in the West African countries to anticipate the outbreak's trajectory at the regional level. This anticipation is based on calibrating a dynamic epidemic model. Its robustness is tested against the basic SIR model. The problem is formulated and solved using a set of nonlinear differential equations. In the second stage, four resource allocation approaches based on greedy, myopic, and dynamic policies are examined for bed allocations, assuming that there are a sufficient number of beds. The performance of these allocation approaches is compared by using training data in different periods and under different budgets. The findings show that the myopic policy performs better than the other methods.

## **6.2. Bioterror Attack in Airports**

Berman et al. (2012) study a resource allocation problem focusing on a bioterror attack on airports. They assume that an unknown number of infected passengers can transmit the disease to other susceptible passengers. They consider allocation of limited resources such as vaccines, human resources and antibiotics to airports in different cities. Given that the number of passengers flying through each airport is different, the objective function is to minimize the total expected number of deaths. They formulate the model with the SEIR model for vaccination embedded in it and use Lagrangian relaxation to solve an approximate version of the model and drive a closed-form solution. They expand their model to minimize the maximum number of deaths.

## **6.3. Staffing in Mass Immunization**

Rachaniotis et al. (2012) study resource allocation of medical teams. The SIR model is used to calculate the disease spread rate. The objective function is to minimize the number of infected people. Borrowing from the scheduling literature, a job's processing time may increase because of a long waiting time before processing. Such jobs are considered deteriorating jobs (Mosheiov, 2005). The case study includes a medical team's assignment to vaccinate older people over 80, who cannot go to the vaccine centers. In reality, a random system was used to vaccinate people with appointments based on telephone requests. This system did not significantly impact the infection rate due to various reasons, including the shortness of the time for administering vaccines. If the proposed assigned medical teams are used, the number of infected people will decrease significantly compared to the random model. The research shows that the number of infected people is not impacted by an increase in the initially infected people.

While Rachaniotis et al. (2012) intend to minimize the number of infected people, Beeler et al.

(2014) optimize staffing decisions by presenting a discrete-event simulation method for mass immunization clinics (MICs) that is important for local authorities. The model considers several scenarios like the peak-capacity (baseline), full capacity and overloaded system. It also adopts realistic aspects of the problem like waiting times (including reneging and balking), and societal/economic losses (estimated as the minimum cost for the waiting times of patients, nurses, etc.). Note that shorter waiting times can also reduce the exposure time and disease propagation rate. The research shows that there is no need to hire additional staff in such situations. If the current staff works at full speed, productivity will be the highest.

#### **6.4. Future Research Opportunities**

Resource management in pandemics/ epidemics has drawn the attention of OM researchers over the past decade. The most popular technique is mathematical programming using largely F&A data. The topics studied include bioterror attacks in airports, staffing in mass immunization, hospital and bed allocation, and vaccine allocation. Since the area is close to the OM community's expertise, OM researchers can contribute significantly to further research.

Investigating surge capacity of hospitals during a pandemic is an important research topic. Evaluation of multiple vaccine candidates when a new pandemic is involved (such as COVID-19) becomes a crucial area for research. This is particularly true when the candidate vaccines' production must occur before each candidate is fully tested, evaluated, and one or more is accepted. Situations where some vaccine candidates require multiple shots before becoming effective while others provide a sufficient level of protection with a single shot only require attention. An important potential OM research topic deals with establishing MICs that might provide a disruptive approach to traditional vaccination programs.

#### **7. Supply Chain Configuration**

There are two review papers in this area which are Dasaklis et al. (2012) and Brandeau (2019). Dasaklis et al. (2012) divide the literature into (i) preparedness, outbreak investigation, response and evaluation, and (ii) surveillance, hospitals/ pharmaceutical and (iii) physical logistics resource allocation. The authors list the details of activities and split the papers along two dimensions: (1) disaster type that includes bioterrorist and natural outbreaks, and (2) timing that includes pre-event, post-event, and integrated. They analyze each paper in terms of objectives, constraints, assumptions, etc. The research shows that most logistics operations papers focus on epidemics logistics network configuration, stockpiling medical supplies, and triage operations.

Brandeau (2019) reviews papers related to preparedness for bioterrorism attacks or disease outbreaks and, specifically anthrax, one of the deadliest forms of biological terrorism. It does not have any indicators (e.g., no color and no smell). Since two antibiotics can be used to prevent the disease, the researcher believes that stockpiling and distributing antibiotics on time is the most effective

solution. The major logistical challenge is not the availability of the inventory nationwide; it is a limitation in the dispensing capacity because in 48 hours all infected people need to have access to the antibiotics. The paper introduces stockpiling strategies at all homes, workplaces, pharmacies/hospitals, and nationwide. Each of these strategies has advantages and disadvantages in terms of cost and response time that can be investigated.

## **7.1. Coordination between Governments and Organizations**

### **7.1.1. Nationwide vaccine SC**

***Influenza vaccine SC:*** Chick et al. (2008) consider a seasonal flu vaccine SC with two players: a government and a manufacturer. The manufacturer produces a vaccine quantity to maximize (minimize) its expected profit (net cost) in an uncertain situation. Like in the newsvendor problem, additional vaccine produced this year cannot be used for the year after, while producing less than the demand results in lost sales. The government considers a fraction of the population that needs to be vaccinated. Accordingly, the government will order an amount of vaccine from the manufacturer to minimize its total cost, including purchasing and health costs. The authors solve the two-player game and show that it has a Nash equilibrium. The researchers assess a contract setting such as wholesale price and payback, and incentives to see if the players can collaborate to reduce their overall financial and health costs. This research shows that wholesale price and payback contracts cannot satisfy the two SC players for their own objectives/ constraints. A special type of cost-sharing and coordinating can improve cost-benefit in public health and provide incentives for both players.

Shamsi et al. (2018) extend Chick et al. (2008) by (i) considering a backup supplier to overcome uncertainties and (ii) adding a new social cost objective. An option contract is developed between a buyer, a governmental organization, and two vaccine suppliers. One of the suppliers is the main supplier with a specific capacity and price. The other one is the backup supplier, which is more expensive but ensures a reliable supply for covering any uncertain demand above the first supplier's capacity limit. The problem is formulated as a Stackelberg game, where the buyer is the leader trying to minimize procurement and social costs (minimizing the infected people and maximizing the recoverable people). The suppliers are followers and maximize their incomes. The main decision variables are the number of orders from the leader to each supplier. Based on the SIR epidemic model, the authors use available data and apply their model to Iran's case. Their findings show that if there is no pre-disaster contract option, the social cost will increase due to the long lead time of vaccines compared to the contract option's lead time. This fact may apply to the buyer's procurement cost to provide the vaccines obtained from national or global markets. The buyer should order from both suppliers to keep the market competitive. This approach will not allow the suppliers to increase their prices.

***Partnership in urgent health services:*** Gibbons and Samaddar (2009) investigate how a government and organizations (e.g., nonprofit organizations and distributors) can form a temporary

partnership network for efficient vaccine delivery. Efficiency is defined as how quickly people can be vaccinated, given the limitation on the available vaccines. They conduct simulations for a city of thousands of inhabitants who need to receive vaccines in a short time. Regarding an appropriate place to be vaccinated, the government can provide advice to people based on a pre-determined priority list or people can randomly search. The results show that forming a partnership between producers and a small number of distributors significantly improves the delivery system's performance. Therefore, the distributors with a higher capacity are not necessarily the best choices to receive a referral. The researchers recommend forming a partnership with a few distributors based on their locations and capacity, and refer patients daily.

**Overlapping disasters:** Rottkemper et al. (2011) investigate inventory relocation in areas affected by a sudden increase in demand due to overlapping disasters. For example, when relief operations were ongoing in the Haiti 2010 earthquake, hurricane Tomas struck. In such situations, some areas may have excess inventories and other areas may face shortages. The authors develop a mixed-integer and linear model in a multi-period setting to decide how much inventory from each region needs to be transported to other areas. The objective function is to minimize cost including transportation, inventory replenishment and inventory holding costs and penalty costs related to shortages and unsatisfied demand. The authors test their model on a realistic example in a vaccination program in a rural area in east Burundi. Due to higher uncertainties about future periods, the authors suggest the model be used on a stepwise rolling horizon basis. The research shows that the solutions obtained from a rolling horizon setting with certain parameters provide higher quality solutions (unsatisfied demand and total cost) than when considering uncertainty.

### **7.1.2. International vaccine SC**

**Containment:** Chick et al. (2008) and Shamsi et al. (2018) investigate a vaccine SC at the national level, whereas Sun et al. (2009) and Mamani et al. (2013) study interrelated issues between several countries. Sun et al. (2009) investigate a vaccine stockpile problem among multiple countries in the case of pandemic influenza. They consider country 0, where the epidemic starts. Each country has a fixed population size and needs to decide how many vaccines to store to minimize the expected number of infected peoples. The research uses a game model to examine how different countries decide about their vaccine stocks if an epidemic starts in a country with little or no vaccine inventory. The decisions are how many vaccines should a country give up to country 0 and how much to keep for its future use. The authors use a multivariate Reed-Frost model to calculate disease spread within a country and across counties and obtain the Nash equilibrium in this game. The findings show that if the transmission rate between countries is low and there is no central planner like WHO, a country (other than country 0) will supply all of its existing drugs to country 0 and not give it up to any other country. Moreover, if there is a central planner, all countries can make a fair agreement on an allocation scheme between them.

***Influenza vaccination:*** Mamani et al. (2013) design a mechanism to coordinate several countries for the allocation of seasonal influenza vaccines by using a game-theoretic concept. Similar to Sun et al. (2009), they assume that the outbreak starts from a source country and calculate the Nash equilibrium. Through numerical experiments, they show that their model reduces overall infection costs and the number of infected people. The research shows that a country should not design its vaccination policy individually; it needs to be based on transmission rates between countries.

## **7.2. Food Home Delivery**

Ekici et al. (2014) investigate food preparation for people who do voluntary quarantine during an influenza pandemic. They apply an agent-based disease spread model to anticipate the disease's spread. Then, a multi-period, multi-echelon facility location problem is developed for food SC network design. The disease spread model is used to find the demand for food. The objective function is to minimize the total costs, including transportation costs. Points of deliveries (PODs) are schools, churches, community centers, and businesses. Demand nodes are households. The main variable is the number of meals sent from supply points to PODs and from PODs to demand nodes. Supply points are grocery stores and charity foundations. Two heuristic approaches are introduced to solve the problem: static (STAT) and dynamic (DYN). The STAT can work well for in-advance planning since it estimates the disease's spread and the demand for food for the initial periods. DYN can be used in the implementation stage as it updates all parameters over time. The solutions are applied to test problems from several counties in the U.S. The research shows that a voluntary quarantine decreases capacity bottlenecks and disruption of the food SC. When shipment cost decreases during quarantine, the total cost will increase compared to the no intervention case. On the other hand, the lower shipment cost will lead to a lower quality of service (defined as the percentage of demand that is satisfactorily serviced served from a POD within 10 miles of the demand location) since more demand will be received from greater distances. Gui et al. (2019) study the effectiveness of various strategies to replenish micro-retailers in remote areas and show the benefits of cooperative strategies for consumer welfare. Such strategies to serve remote areas gain importance for pandemics and other extreme disasters.

## **7.3. Logistics and Physical/ Psychological Fragility**

He and Liu (2015) investigate how physical and psychological fragility can be reduced in epidemics. Physical fragility is a function of the amount of emergency supplies sent to a specific group of people. The more items supplied to meet demand, the lower is physical fragility. Psychological fragility is the fear generated in people from different groups who are susceptible or exposed and infected. They modify the SEIR model and use it to decide the optimal amount of medical supplies dispatched from each emergency medical reserve center to each of the affected areas in a multi-period setting. The objective function is to minimize physical fragility. The authors then extend the model to minimize

psychological fragility measured based on unsatisfactory amounts of treatment relief. The model is solved by using commercial software and tested on real data related to SARS in China. This research shows that survivors' psychology can significantly improve psychological fragility for the affected people.

#### **7.4. SC Network Design in Developing Countries**

##### ***7.4.1. Niger vaccine SC***

Based on the WHO's Expanded Program on Immunization (EPI), Chen et al. (2014) study a vaccine SC in developing countries and investigate how it can be designed to work more efficiently. The current vaccine SC has four levels, which are expanded from national, regional, district and clinical levels to reach recipients. At each level of the vaccine SC, there is a limited capacity of facilities such as refrigerators and freezers that can keep the vaccine for a long time. The authors suggest a linear program model to optimize inventory and distribution decisions in the vaccine SC. The model's objective function maximizes the number of Fully Immunized Children (FIC) plus additional vaccines to be stored in the locations that have spaces. The authors also expand the model by including minimization of the total capacity investment cost. The model is tested in the Niger's vaccine SC network to analyze scenarios such as removing a distribution level, changing vial size, and introducing new vaccines and capacity expansion. The research shows that removing a level in the SC, namely removing the regional stores, does not significantly improve the efficiency of the existing SC network.

##### ***7.4.2. Healthcare SC network in Haiti***

Anparasan and Lejeune (2018) and Anparasan and Lejeune (2019) study a location-allocation problem in Haiti based on data from the cholera epidemic after the Haiti 2010 earthquake. The first paper introduces a dataset that contains information about the number of geographic locations of patients and location/capacities of hospitals (e.g., the number of staff) for 120 days. Anparasan and Lejeune (2019) use this dataset in an integer linear programming (ILP) model to determine the number, size, and location of healthcare facilities, location of ambulances in triage points to transport infected patients to treatment facilities. The objective function maximizes the number of infected people transported from triage to treatment centers. There are three types of treatment facilities that differ in capacity and range of treatments. The main constraints are the number of medical staff and the earmarked monetary donations to open new treatment centers. The authors suggest several families of valid inequalities to hierarchically cut some sections of the feasible regions and speed up computational time. They compare the results of their model with other prevention strategies in the literature, including antibiotics, vaccinations, and provisions for clean water, in terms of death rate in each scenario to show the efficiency of the suggested model.

## **7.5. Future Research Opportunities**

The research studies in this section investigate mass dispensing, vaccine SC coordination, food home delivery for the quarantined, and SC network design. The trend in SC configuration of modeling is similar to what is observed in ‘mitigation’ problems. The field has attracted attention for a decade. Various data types and analyses techniques have been used but mathematical modeling and F&A data are significantly more popular than the others.

There are many possibilities for future research in pandemic SCs. We focus on two groups of vital items in medical SCs (e.g., vaccine and medication) and foods. The related SCs are global in which a number of nations are involved. Research is to determine if a country needs to optimize its resources at the outset of a pandemic and not share it with other nations. On the other hand, this approach may damage trust and long-term relationships in SCs. Keeping balance in such a situation can help to identify various research gaps. For example, countries locally can apply limitations to their import and export activities and may not be able to run their global SCs freely. When it comes to a domestic SC, last-mile delivery is the bottleneck. Research can help determine how to dispense food or medications best (e.g., how to deal with the distribution of a new vaccine). Research is warranted to better coordinate and integrate many public and private organizations' activities to optimize their potential abilities and skills for quickly dispensing new technologies and medicines. An attractive domain for future research exists in the intersection of psychological and physical fragility.

## **8. Decision Support Systems for Managing Pandemics/Epidemics**

### **8.1. Mass Dispensing in Infectious Diseases**

Lee et al. (2006) develop a DSS for large-scale dispensing of medications in case of a biological attack and infectious disease outbreaks. The DSS uses an integer programming model for clinic design including its layout design and staffing. Modular design with possible scenarios in each module such as patient arrivals, triage, and orientation of rooms are considered. Efficiency measures such as the most efficient floor plan, the most cost-effective dispensing, and the smoothest operations (i.e., shortest average wait time, average queue length, equalized utilization rate) are evaluated for a combination of scenarios to choose the best one. The DSS is tested and validated, including what-if analysis, on an actual anthrax-treatment and smallpox vaccination using 864,000 households in Atlanta, USA.

In contrast to Lee et al. (2006) which is dedicated to medications, Fogli and Guida (2013) propose a knowledge-centered DSS that can be used during a pandemic alert, pandemic, and post-pandemic periods. An emergency scenario is defined by various factors such as population size, institutional participation, operational involvement, and emergency management units. The DSS architecture has three layers: knowledge and data layer, application, and user interface. In the knowledge and data layer, database, document-base and knowledge-base exist. In their experiments, the authors implement their suggested DSS on a prototype to provide surveillance of a flu pandemic



in Italy.

## 8.2. HIV/AIDS

Rauner (2002) designs and implements a DSS for resource allocation for HIV/AIDS control programs that works based on a system dynamics model and simulation. The system dynamics model consists of several compartments showing different populations in terms of their health situation (infected or non-infected), gender, age, behavior (i.e., intravenous drug user, homosexuality, or prostitution), testing status, etc. and the ways the virus is transmitted from one group to another. The authors successfully tested their model based on real data in Vienna, Austria, to achieve cost-effective solutions for drug treatment, additional therapies and HIV screening. The DDS can help a local government analyze various resource allocation scenarios and decide how to proceed based on the possible consequences.

Following Rauner (2002), Rauner et al. (2005) design a discrete-event simulation model to evaluate two intervention strategies with different fixed and variable costs and benefits: (1) anti-retroviral treatment (ART), which is applied at childbirth, and (2) bottle feeding instead of breastfeeding. ART needs a combination of medicines, which is not a cure but can help infected people live longer. Bottle feeding is a replacement for breastfeeding – and can increase mortality compared to breastfeeding (Coutsoudis et al. 2012) – that can be applied at delivery, at three months, or six months. The authors model the problem, using systems dynamics modeling– by splitting the population in terms of their age, maternal stage (pregnant or breastfeeding), etc. – and solving it using a Markov chain simulation. The model is tested on data from rural Tanzania.

Heidenberger and Flessa (1993) explain that the pattern of AIDS in sub-Saharan Africa (so-called pattern 2) is different from HIV in the United States (so-called pattern 1). In pattern 1, male homosexuals and drug users are mainly involved. In pattern 2, HIV is mostly diffused through heterosexual intercourse. Unlike pattern 1, in pattern 2, children are also involved through their mothers and contaminated blood in hospitals. Besides, most of the population in pattern 2 live in rural areas (around 75%). Four layers are defined for the population: level 1 (age, sex, urban, and rural areas), level 2 (children), level 3 (healthy, HIV+ and AIDS; HIV+ is further divided into short or long incubation period), and level 4 (time since the acquisition). The links between groups over time have been considered. Based on data from the literature and survey in Tanzania and opinions of AIDS experts, a system dynamics model is used to learn how the transmissions happen among different groups. The model can evaluate the efficacy of intervention strategies and forecast future strains for resource allocation.

Harper and Shahani (2003) design a DSS for predicting the future number of HIV/AIDS patients. The DSS works based on a simulation model and considers the historical chronology of different subgroups/ populations as asymptomatic, early stage, intermediate stage, and AIDS. Then, it helps practitioners analyze various scenarios for the provision of effective care based on healthcare costs.

The model has the flexibility to accommodate some changes. For example, in the case study, high-income and low-income groups are separated. Also, in the case study, the DSS estimates the required budget for a clinic over the next ten years.

### **8.3. School Closures**

Araz et al. (2013) design a DSS to investigate the problem of school closure planning in the case of a pandemic. WHO recommends school closure in the early stages of a pandemic. This is a challenging decision due to its direct and indirect economic impact, such as student meals and education delivery. The authors consider an area with several counties and various types of schools in each county, including preschool, elementary school, middle school and high school. A disease can be transferred from one county to another and also between schools in a county. The authorities decide between (i) early closure/ limited re-opening and (ii) sequential closure/re-opening to minimize (1) the total number of infections in the schools and (2) discontinuity in education. The authors use the SEIR transmission model and employ simulation to analyze it based on an exercise scenario and implement it on data from the 2009 A/H1N1 influenza outbreak in Arizona, USA. The findings of their research show that decision (ii) is preferred.

### **8.4. Community-based Collaboration**

Li et al. (2014) suggest setting up a collaborative information system in emergencies but the authors believe the system can help in a disease outbreak. The research suggests using an information system to maximize the utilization of the available resources. The system is community-based and uses a Multi-Criteria Decision Making (MCDM) tool. Stakeholders such as local authorities, NGOs, police and fire departments, public and private organizations in a community share their data in a “ground zero” situation. Such a system can help increase awareness, mobilize, and make appropriate decisions based on local knowledge and resources. In designing the system, the authors adopt the W3C Emergency Information Interoperability Framework which stands for “who-what-where.” In this taxonomy, stored data such as capabilities, resources, and locations are acquired from appropriate organizations in the communities. A pilot is implemented to show the system can collect and integrate information for mass collaboration based on some data from EM-DAT and some randomly generated data.

### **8.5. Crowdsourcing**

Han et al. (2019) investigate the integration of crowdsourcing and the Internet of Things (IoT) which brings together social media and RFID technology in disaster response by a simulation model. While the focus of the paper is not on epidemic/ pandemic outbreaks, the authors perceive similarities between the SIR model and disaster response. They urge researchers to investigate its application in disaster response.

### **8.6. Foot-and-Mouth Disease**

Ge et al. (2014) develop a decision support framework for foot-and-mouth disease (FMD) which arises from livestock production. The framework works at the strategic, tactical and operational levels, so-called multi-level hierarchical Markov processes (MLHMP) and is applicable to contagious diseases such as classical swine fever and avian influenza. Decisions made at each level depend on the higher level. The level of uncertainty in the lower decision-making levels is less than in the higher levels. The decisions and states can be time horizons, stage lengths, level-specific actions, etc. Strategic processes involve decisions about using preventive vaccination. Tactical levels involve implementing additional measures (e.g., pre-emptive culling), emergency vaccination or implementing compulsory measures. The operational level decides whether to start or continue the program. To solve the problem under uncertainty, a Bayesian forecasting method is implemented that is based on learning over time.

### **8.7. Future Research Opportunities**

The DSS discussed in this section focus on mass medical dispensing, resource allocation, disease prevention or slowing down disease transmission, school closures, community-based collaboration, crowdsourcing, and emergency vaccination. Disease-specific research mostly focuses on HIV/AIDS, H1N1, anthrax, and smallpox. Simulation is the most popular technique in the model base because it provides the ability to conduct scenario analysis. Moreover, the related databases are supported by F&A. In the future, the increasing power of computers and availability of data generated through information technology will create stronger DDSs.

We observe that medical DSSs for managing pandemics/epidemics are highly developed for HIV/AIDS because there are rich databases for various countries. Extending such DSSs for other diseases has not been accomplished. For example, this model might be useful for observing the impact of a vaccine or a disease suppressor (neither of which yet exist). Another research opportunity is to develop robust quantitative DSS models. Currently, the predominant models use system dynamics and simulation as their primary technique. An important aspect of designing an efficient DSS is computational time, as we are dealing with complicated models and large databases. Therefore, developing efficient solution techniques is critical, particularly with a DSS that requires rapid operational decisions compared to strategic decisions involving long planning horizons.

Providing what-if analyses is an important feature embedded in some research studies. This needs to be continued to cope with uncertainties. Only one of the papers in this section uses an MCDM technique which is appropriate to observe the changes in conflicting criteria when evaluating various scenarios. In the future, researchers can increase their effectiveness by efficiently solving DSS models combined with MCDM techniques (Gutjahr and Nolz, 2016). Research should also be extended to surveying and extending models that can effectively determine the effectiveness of

various vaccines. As was previously noted, such analytics do not yet exist for vaccines or for various disease suppressors.

## **9. Risk Assessment**

### **9.1. Performance Measures for HIV/AIDS**

Zanakis et al. (2007) assess the efficiency of 116 countries in controlling HIV/AIDS. They investigate the relationship between economic development, migration and the nation's health performance with HIV/AIDS epidemics. The researchers consider many independent variables and shortlist dependent and exploratory variables. They apply data envelopment analysis (DEA) to assess each country's output based on their inputs. The research findings show that nations with lower population density provide better health performance and superior per capita support. Nations that are not rich but still have high performance provide better media information and lower HIV/AIDS indicators. The authors suggest a multi-national collaboration to improve performance measures for the HIV/AIDS pandemic.

### **9.2. Social Amplification of Risk**

Busby and Onggo (2013) investigate the concept of social amplification of risk that does not explicitly focus on disease outbreak but it can be used for that purpose. The research deals with social processes where risk perception is exaggerated or underestimated. The authors use system dynamics to model this qualitative problem for risk perception and risk communication. They develop three models: the traditional view based on social risk amplification (basic model), adding an attributional subsystem to the basic model, and adding complexity to the basic model. Real data are collected from people involved in studying zoonotic outbreaks. These people are divided into an expert group and a lay group. The findings show that expert people systematically find explanations to exaggerate or underplay their views. Neither group tries to correct their own initial beliefs. Therefore, social amplification based on subjectivity in different actors magnifies polarization.

### **9.3. Ebola Risk Assessment**

Powell et al. (2018) study the role of systems knowledge in identifying and assessing risk, focusing on the Ebola outbreak. The authors believe that comprehensive systems knowledge should include dynamic behavior, the role of human agents, and the availability of knowledge to the agents. Accordingly, they suggest a system to comprise these factors contrasting, information, knowledge used in a system, knowledge about the system and the knowledge placed in a system. The researchers suggest a procedure that works based on influence diagrams and system dynamics as a qualitative technique to identify risks and suitable risk management policies. Based on data from the Ebola outbreak in West Africa, they show how the procedure works and explain its usefulness.

### **9.4. Future Research Opportunities**

In this section, the papers that study risk assessment in pandemics/epidemics focus on HIV/AIDS and Ebola in one or more nations. DEA and system analysis are the preferred techniques. Risk assessment for pandemics/epidemics by OM scholars is an under-explored area. The existing research is mostly at a national level (except one). In the future, we need more global research in which different countries are compared and contrasted.

Possible research could focus on applications in a single country or across multiple countries. In single-country research, risk assessment is closely linked to social and behavioral aspects which are difficult to quantify. That is why existing papers use qualitative data analysis methods. Research across several countries is illuminating as it compares and contrasts actions taken by various nations in controlling an outbreak. Techniques used for measuring productivity such as DEA can be reasonable. However, research in the field requires a high volume of empirical data that may not be readily available. Further, there may be issues with data accuracy as different nations have different transparency levels leading to invalid analyses. Of great potential value is research on the effects of bias wherein experts provide explanations that systematically amplify or underplay the seriousness of situations.

## **10. Implications for Managers**

Most of the research reviewed in this paper is based on real-life case studies; and real and archival data. Therefore, the research is practical, useful, and impactful for everyone in the world. However, COVID-19 is a different beast and a dangerous one; more furious than a category five hurricane. The current generation has not experienced a pandemic of this size before. The whole world is engulfed in the fury of this disaster. To list a few, never before, anyone has witnessed school closures, business closures, ban on national and international travels, and the complete lockdown of some countries for months. Vaccine is not available and its distribution logistics is not known. Because of the shutdown, providing food and groceries to households has gained significant importance. Hospitals are not able to manage the surge in demand.

Since COVID-19 has impacted all lives around the world, everyone becomes a stakeholder in sharing the benefits from pandemic research. However, we have grouped stakeholders into the following categories: National Policy Makers, Healthcare (including hospitals) Administrators, Business Executives, School Administrators, and Researchers. In Table 1, we list various issues that are important for these stakeholders based on the lessons learned from the models, frameworks and empirical studies available from prior research; and the research directions provided in Section 11, Conclusions and Future Research Directions.

Table 1: Stakeholders and Relevant Issues

Stakeholder	Relevant Issues
National Policy Makers	Business closures, school closures, mitigation and interventions, lock-downs, impact of national culture, food stockpiles, social unrest, travel restrictions, global and domestic vaccine contracts, insourcing/ outsourcing vaccine production.
Healthcare Administrators	Monitoring warning signals, disease prediction, disease spread, healthcare policies, vaccine development, vaccine stockpiling and distribution, hospital capacity and bed allocation, mitigation strategies, mass dispensing and immunization, health-related donation, treatment prioritization, co-epidemics, and the ability to understand and deal with risk amplification.
Business Executives	Implications of dividing businesses into essential and non-essential, SC for vaccines, knowledge of how to ramp up manufacturing capacities, logistics of food home delivery, bioterror through commercial SC
Educational Administrators	Education delivery (online, face to face, hybrid), class schedules, international students, management of dorms including food services
Householders	Medicine home stockpiling, quarantine and shielding, community-based collaboration, knowledge of how to assist disease tracing
Researchers	All issues listed above and described in detail in Section 11, Conclusions and Future Research Directions

## 11. Conclusion and Future Research Directions

Our review of research on pandemics/epidemics identifies research problems, research questions, data types, data analysis techniques, and disease types, therapeutics and vaccines. The research findings and future research directions are discussed in each section. In addition, we discuss below potential research topics that are important in the short run to manage COVID-19, and future pandemics in the long run. We have divided our recommendations into the following groups: (A) Disease Prediction, (B) Mitigation and Interventions, (C) Socio-political and Economic Consequences, (D) National Culture, (E) Resource Planning, and (F) Analytical Techniques.

### A. Disease Prediction

Most of the papers discussed in our review are disease specific and are likely to become part of archives having only historical significance once the disease is eradicated. However, their research findings can be extended to predict and cope with future diseases. As we learned, the original SIR models were extended to SEIR, and SIS, etc. New models are required for the COVID-19 pandemic. For example, a forced Susceptible-Exposed-Infected-Recovered-Dead (fSEIRD) model implemented in Italy is claimed to be more realistic for this disease (Piccolomini and Zama 2020). New prediction models are required as COVID-19 still persists and its duration is uncertain (Scudellari 2020). The spread of COVID- 19 appears to be going in waves. Yet, this description is controversial because variables such as weather and various lock-down rules may be seen as factors that modify the same single onslaught of the disease over time and various places. It is important to study all relevant factors that lead to this variability to predict an end.

- Current models mainly study the containment of outbreaks at national or community levels.

Building trust and collaboration between countries could contain the outbreak and mitigate consequences (McCloskey et al. 2014).

- The existing disease spread models are mostly at urban levels. There are some community-based models where a community is defined based on disease type (e.g., HIV community). COVID-19 revealed that there are many confined communities (e.g., universities) that need models to support their decisions such as crowd sizing (identifying event crowd-size restrictions for different groups, e.g. in university or school), university start time, hospital surge planning etc. (Kaplan 2020).
- Demographics play an important role in susceptibility, as well as which agents spread diseases. It appears that various population segments have superior immunity to symptoms and are therefore efficient asymptomatic carriers of contagious diseases. Who are they? Different disease patterns apply to various age groups, blood types, DNA characteristics, and gender. This is a research domain (medical, pharmaceuticals and OM-oriented) of great significance which must include the impact of enormous technological change that is likely to accelerate in the near future. Cooperative multi-disciplinary efforts need to be brought to bear and research is warranted on how to achieve this goal.

## **B. Mitigation and Interventions**

Pharmaceutical and non-pharmaceutical interventions are essential to contain the spread of disease. OM researchers will find many important and interesting avenues for research in this area.

- Vaccine development lies in the domain of medical research. However, after a safe and effective vaccine is developed and approved by the authorities (e.g., Food and Drug Administration in the U.S.A.), OM researchers can make contributions by analyzing a variety of related problems that fall within the domain of capacity planning and logistics. For example, the optimal quantity of vaccine to be manufactured needs to be estimated. Manufacturing facilities must have appropriate capacity to produce these vaccines on both, regional and global levels. Underproduction will leave populations unprotected; over-production will lead to unnecessary cost, increased hazardous waste, and severe opportunity costs for misplaced efforts. This production capacity, released by reducing overproduction, could have been allocated to developing beneficial pharmaceuticals. Allocation of vaccine among different countries, to different regions within a country, and among different segments of populations (by age, ethnicity, and medical conditions) needs to be determined. Logistics of distribution and SC management are also important so that the vaccine reaches those who will benefit the most as quickly as possible. In preparation for research along these lines, it will be useful to read more about vaccine allocation and distribution issues in Branswell (2020) and WHO (2020).
- Timing of non-pharmaceutical interventions is important to contain pandemics and is an important research topic. Governments around the world assessed the potential for harm in different ways and employed different strategies considering their culture, political orientation, skills and resources to mitigate the impact of the pandemic (Akpan 2020; Galloway 2020). Some governments swiftly forced

lockdown strategies at early stages while others did not enforce such measures or did so at later stages. Some countries started mass testing of those suspected of being infected and others advised people to delay treatment for days after experiencing symptoms due to lack of healthcare resources and/or test kits. Some authorities distributed PPE (personnel protective equipment) (such as N95 masks) among frontline healthcare providers, some enforced quarantine regulations, and some started to construct new hospitals at very early stages. Obviously, at the international, national and state levels, there has been a clear lack of proven plans in place at strategic, tactical and operational levels to be implemented effectively. Study of these issues is essential to develop effective national policies to cope with pandemics.

- Decisions regarding closing and reopening of educational institutions, including universities and K-12 schools, need to be systematically investigated with respect to all relevant variables. We have not found any substantial efforts in this regard. In particular, school and nurseries' closure may affect working parents, teachers, and a variety of adults who interact in different ways with each particular situation even if their business is still running (Chin et al. 2020).
- Impact of travel restrictions within a country and across country borders needs more investigation.
- Acquiring precise and quick knowledge about the nature of diseases in terms of (i) being viral or bacterial, incubation period, transmission mode (e.g., airborne or droplet), etc., (ii) existence or lack of a vaccine before infection, and (iii) existence or lack of treatment after infection are pre-requisite for the members in a healthcare SC. Then, practitioners in the related SC can utilize OM concepts to decide about inventory, staffing, mass vaccination, and so on.

### **C. Socio-political and Economic Consequences**

COVID-19 has far reaching social, political and economic impacts. A study of these impacts is essential to minimize adverse effects on society and economy.

- Social unrest, likely to be created by a pandemic, is an important research topic. A pandemic was the cause of ‘collapse of social cohesion’ as discussed in section 4.5 (Carvalho-Rodrigues et al. (1993)). If COVID-19 is not contained, it may lead to societal breakdown; and create social and financial crises. Research shows that “the probability of riots, violence against civilians, food-related conflicts, and food looting has increased since lockdowns” (Roxana Gutiérrez-Romero 2020). Psychological impact of a pandemic is an important research topic. In preparation for research along these lines it will be useful to read more about social unrest due to COVID-19 (Tomic 2020; Galea and Abdalla 2020).
- Economic impact of business closings is an important research area (Atlas et al. 2020 and Porter 2020). The research issues include among others: determining times for closing and reopening, impact on employees’ morale and financial status, impact on small as well as large business owners, conditions under which various businesses will be closed, and requirements to be fulfilled for



reopening. There is also the extent to which employees work from home and how that condition persists after re-opening.

- Managing COVID-19 seems to have become a socio-political issue, at least in the U.S.A. How does the political governance system influence decisions and plans to contain the spread of the disease? The study of the decision-making style of political leaders is important. Carey (2020) has found that nations with female leaders performed better than others in combatting the COVID-19 pandemic. More research is needed to test the assertion that the gender of a country leader may affect the control of disease spread.

#### **D. National Culture**

- Compliance with recommended or mandated non-pharmaceutical interventions, like social distancing, wearing masks, quarantining, isolation, contact tracing, etc. will be different across nations because of national culture (Gupta and Gupta, 2019). Impact of culture on the enforcement of such decisions needs to be studied. Also, there are contradictory opinions about the effectiveness of these measures on disease spread. Some believe that these opinions are politically driven; others contend they are data driven. Research is needed to bridge this gap.

#### **E. Resource Planning**

- Building surge capacity for healthcare resources is an important topic for research. For example, shortage of ventilators, ICU beds, PPE during the initial phases of the COVID-19 pandemic was a major problem faced by hospitals in the U.S.A. as well as many other parts of the world. During COVID-19 the hospitals are dealing with pandemic as well as regular patients. Distribution of hospital capacity among these two groups is an important area of research. Klein et al. (2020) provide a systematic review of many existing surge capacity models and show that just a few of them can help healthcare systems respond to COVID-19 or similar pandemics in a practical way.
- Study of SC disruptions, particularly in the food industry at the retail level is important. Grocery deliveries to households have become an important fallback during the pandemic. How to stockpile food supplies is an important area of pandemic research.

#### **F. Analytical Techniques**

- Stochastic modeling and statistical analysis have been frequently used at tactical and operational levels. *Simulation* was used for prioritizing treatment, staffing decisions at mass immunization, vaccine allocation, school closures, treatment policies, disease spread, mass dispensing of medications, DSS design, and resource allocation. *Stochastic modeling* was utilized in disease progression, DSS design, vaccination prioritization and quarantine programs. *Statistical analysis* was used in insourcing/ outsourcing, predicting social response, outbreak detection/ early warning, DSS

design, and socio-economic studies.

- However, the problem at hand is very complex and an optimization model may not be sufficient. Applications of systems dynamics and system simulation need to be explored. Appropriate decision support systems have to be developed that can provide decision-making tools for administrators. Interestingly, unlike what is observed in other disasters (Gupta et al. 2016; Gupta et al. 2020), most pandemic/epidemic research is based on primary or secondary data. Therefore, these datasets can also support empirical research in the future. Application of new techniques like machine learning, text data mining, and artificial intelligence (AI) methods taken broadly, need to be explored. Perhaps, the main change over recent years is the availability of internet-derived large databases as the source of empirical data. So empirical research to discover “clusters” in models can help. For example, a cluster of people from a certain religious group could be linked to a specific church in South Korea. Such empirical data can also help develop more advanced machine learning and data mining techniques such as clustering, dimensionality reduction, structured prediction, anomaly detection, artificial neural network analyses, etc.

- Information technology is much more advanced now than it was during past pandemics. We have an opportunity to harness the power of computing, data availability and mathematical modeling to analyze these very complex problems (Keskinocak and Savva 2020). We have previously discussed some information technology applications in pandemic/epidemic research such as DSS and surveillance. These applications can be extended, for example, in containment and mitigation stages. It is important to trace movements of some of the infected people to identify the affected clusters to which they belong. The movements and contacts of infected people can be traced back through their mobile phones and credit cards. However, this raises privacy issues. POM research needs to examine tradeoffs between better health and less privacy. Importance of developing DSS in real time (called scratch modeling) has also been stressed by Kaplan (2020). Abundance of data generated through information technology can support data-driven models, for example, to forecast disease transmission (Paiva et al. 2020).

In conclusion, we assert that managing pandemics/epidemics is a very complex endeavor because medical, political, social, demographic, cultural, healthcare (including assisted living communities) and behavioral factors interact with each other. Multi-discipline collaboration between experts in a variety of interactive fields, with POM researchers at the center stage, can generate effective and efficient alternatives. We also suggest undertaking focussed surveys on the issues raised in this section and including journals from all relevant disciplines.

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## APPENDICES

### APPENDIX A: Pandemics/Epidemics – A Historical Perspective

The human race has witnessed and overcome many deadly pandemics over the last several hundred years. “*Cholera, bubonic plague, smallpox, and influenza are some of the most brutal killers in human history. And outbreaks of these diseases across international borders, are properly defined as pandemic, especially smallpox, which throughout history, has killed between 300-500 million people in its 12,000 year existence.*” (MPHonline, 2020b). Ten of the world’s deadliest pandemics include the following: disease name, (year, estimated death toll), Antonine Plague (165 AD, 5 million), Plague of Justinian (541-542, 25 million), The Black Death – Bubonic Plague (1346-1353, 75-200 million), Third Cholera Pandemic (1852- 1860, 1 million), Flu Pandemic (1889-1890, 1 million), Sixth Cholera Pandemic (1910-1911, 800,000+), Flu Pandemic (1918, 20-50 million), Asian Flu (1956-1958, 2 million), Flu Pandemic (1968, 1 million), HIV/AIDS Pandemic (identified in 1976, 36 million since 1981) (MPHonline, 2020b). Some of the more recent outbreaks include SARS in south China (severe acute respiratory syndrome) between 2002 and 2004, 2009 swine flu in Mexico City, Ebola in West Africa between 2014 and 2016, and cholera (after the Haiti earthquake between 2010 and 2019). COVID-19, declared to be a pandemic by World Health Organization on March 11, 2020, is an ongoing pandemic. The pandemic, with its origin in China, is also known as coronavirus. The virus spreads through air, droplets and aerosols, usually when people are in close distance. Figure A1 shows the growth in number of pandemic cases world wide since its outbreak.

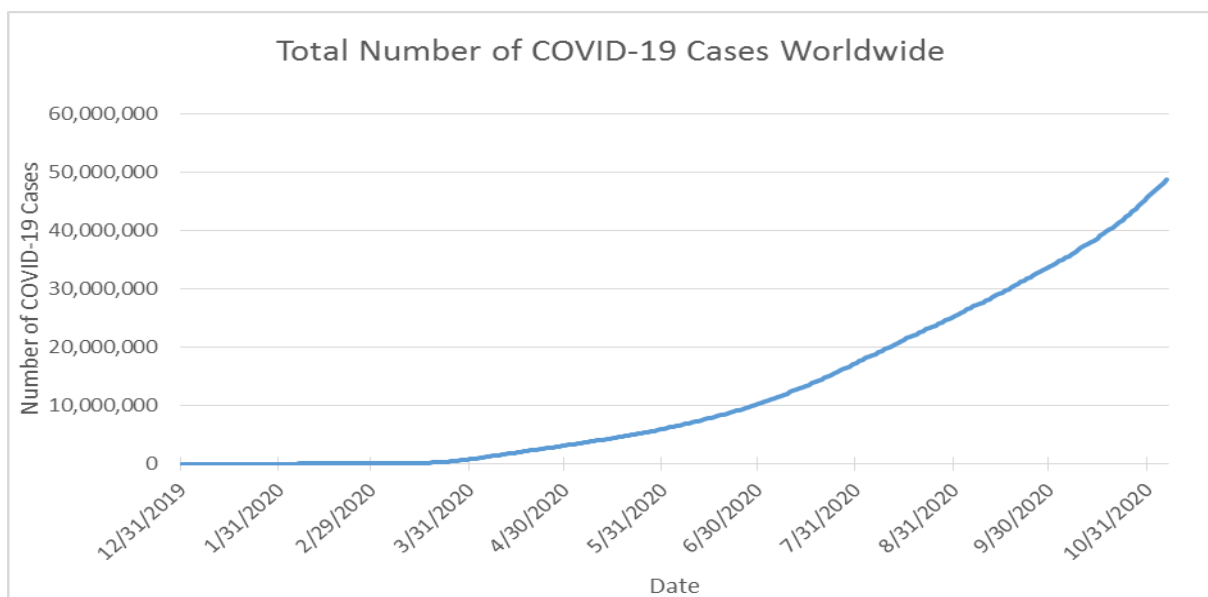


Figure A1: Total Number of COVID-19 Cases Worldwide

Source: Our World in Data; <https://ourworldindata.org/coronavirus-source-data>

Downloaded on November 6, 2020

### APPENDIX B: Description of Diseases

Diseases are caused by pathogens that include bacteria, viruses and parasites. Since 1970, over 1,500 pathogens have been discovered; 70% of them originated from animals (WHO, 2018). Smallpox, different types of flu, measles, hepatitis, rabies, Ebola, HIV/AIDS, SARS, Ross River and Foot-and-mouth disease (FMD) are examples of diseases caused by viruses (Medical News Today, 2017)). Cholera, anthrax, plague, tuberculosis and cutaneous leishmaniasis are examples of diseases caused by bacteria (Stevenson, 2020). Unlike bacteria, viruses cannot survive without a living host. Only some bacteria are harmful but most viruses can cause disease (HealthyMePA, 2017)). A discussion of pathogens and the diseases caused by them can be found in Alberts et al. (2014). In our



study, we found 51 papers that focus on viral diseases, 9 papers on bacterial diseases, 2 papers both (viral or bacterial) and 18 papers discuss general diseases. Thus, 80 diseases are discussed in 75 papers; the discrepancy is because some papers study more than one disease.

Of the virus-based diseases, the first disease-specific paper on swine flu (H1N1) was published in 1983. We observe that HIV/AIDS (16 papers) and influenza (14 papers) have drawn the most attention of researchers. From Table A1, in Appendix A4, we also note that investigating HIV/AIDS has interested researchers since it was clinically observed in the early 1980s. Swine flu research received attention in 2012 after the swine flu pandemic in 2009. Similarly, Ebola attracted attention after the Western African Ebola epidemic (2013–2016).

Of the bacteria-based papers, we found one paper on plague, three on anthrax, two on cholera, and two on tuberculosis. Most of these diseases have existed for centuries so we include here a brief history of these diseases. Plague (aka Black Death) is caused by rodent fleas biting humans (See details in plague, 2020). The outbreak of plague started in the 14<sup>th</sup> century and continued until the 17<sup>th</sup> century. The paper on the plague uses the data recorded during those centuries and its focus is on the collapse of some societies due to the plague (Carvalho-Rodrigues et al., 1993). Cholera has existed for many centuries, but its outbreak in India in 1817 brought the disease to prominence (History.com, 2017). This outbreak was followed by several cholera pandemics killing millions of people around the world. The seventh cholera pandemic includes South Asia (1961), Africa (1971) and the Americas (1991). The most recent cholera outbreak in Haiti in 2010 gave impetus to research on cholera outbreaks (WHO, 2019). Cholera is considered to be endemic in many countries. Endemic relates to an infection that is constantly maintained at a baseline level in a geographic area without external inputs.

Anthrax and tuberculosis are also ancient diseases dating back to the era before Christ (B.C.). The study of anthrax is important because it has been observed in some areas sporadically (e.g., a few cases in the UK among heroin addicts in 2009). Moreover, it is one of the deadliest diseases which can be developed in simple laboratories making it a potential weapon for bioterror attacks (Brandeau, 2019). The history of anthrax including its attack on America in 2001, can be found in CDC (2016). The history of tuberculosis can be found in Barberies et al. (2017). A vaccine for tuberculosis is now available and it is no longer considered to be a major threat. However, it is still important because of the simultaneity of co-epidemics between HIV and tuberculosis. More research papers can be found on each one of these diseases in epidemiology and public health journals. Some of the important journals from these disciplines include: American Journal of Epidemiology, American Journal of Public Health, Annual Review of Public Health, Bulletin of The World Health Organization, Clinical Epidemiology, Emerging Infectious Diseases, Emerging Microbes and Infections, Epidemics, Epidemiologic Reviews, Epidemiology, European Journal of Epidemiology, Eurosurveillance, Health Services Research Journal, International Journal of Epidemiology, Journal of Clinical Epidemiology, Journal of Epidemiology and Community Health, Morbidity and Mortality Weekly Report (MMWR), Preventative Medicine, The Lancet.

For all contagious diseases, the elapsed time between exposure to a pathogen and the appearance of its symptoms is called the incubation period. Incubation periods vary depending upon the type of pathogen. For example, incubation periods are 2 to 21 days for Ebola, 7 to 10 days for Lassa fever, less than a week for Zika, 1 to 5 days for seasonal/pandemic flu, 2 to 14 days for MERS, 2 to 3 days for Cholera, 24 hours for Plague (WHO, 2018). The range of estimated incubation periods for COVID-19 is from 2 to 14 days; it is on average 5 to 6 days (Worldmeters 2020b). The longer the incubation period, the more dangerous is the situation because an infected person is not aware that he or she has been infected, and is therefore more likely to infect other people who have not yet been infected (classified as susceptible).

## APPENDIX C: Classification Frameworks

There is no accepted scheme or framework for classifying research on pandemics. Frameworks differ across countries and across professional/health organizations. The classifications are also influenced by type of virus. For example, in the case of COVID-19, the UK National Health System (NHS) defines the phases as Contain, Delay, Research, and Mitigate (Commons Select Committee, 2020). The World Health Organization (WHO), in the case of the 2009 pandemic H1N1, used the following phases (i) predominantly animal infections and few human infections, (ii) sustained human-to-human transmission, (iii) widespread human infection (pandemic), (iv) possibility of recurrent events (post-peak) and (v) disease activity at seasonal level (post-pandemic) (WHO, 2009). In fact, WHO may release a phasing scheme for major pandemics by the nature of a virus. WHO defines the life cycle of a virus and its outbreak as follows (WHO, 2018): introduction/emergence, localized transmission, amplification, and reduced transmission immunity. For managing pandemics, the WHO suggests the following response interventions (WHO, 2018): Anticipation; Early detection; Containment; Control and mitigation; and Elimination or Eradication.

## APPENDIX D: A Macro-Level View of Pandemic Research

We searched the literature using the keywords “Epidemic(s) or Pandemic(s) or Outbreak(s)” in the top operations management, operations research and management science (OM/OR/MS) journals listed in Gupta et al. (2016). We used SCOPUS as the search engine and looked for the keywords in the title, abstract and keywords of the articles. Our search spans from 1957 (the year in which the first issue of Management Science was published) through 2019. We found 107 papers and selected 75 of these papers for review in this paper. The list of the journals, the number of papers found in each journal are given in Figure A2.

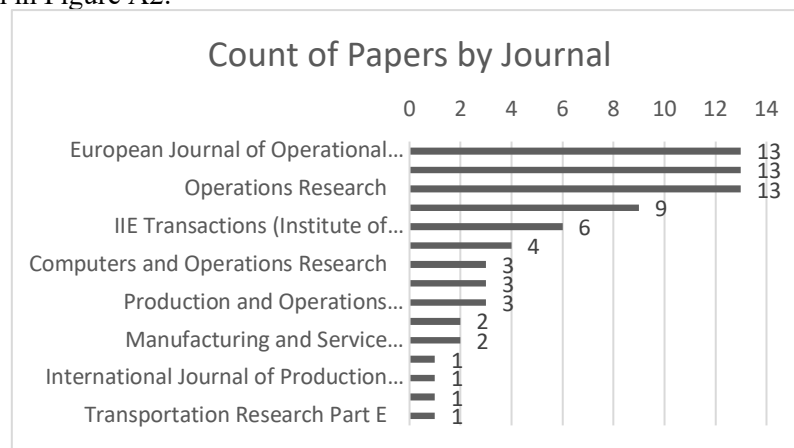


Figure A2: Count of pandemic/epidemic papers in the journal.

The three-year moving average of the count of published papers, in Figure A3, shows the growth trend of pandemic research. This figure shows that researchers in the OM/OR/MS community started investigating the field of epidemiology in the late 1970s.

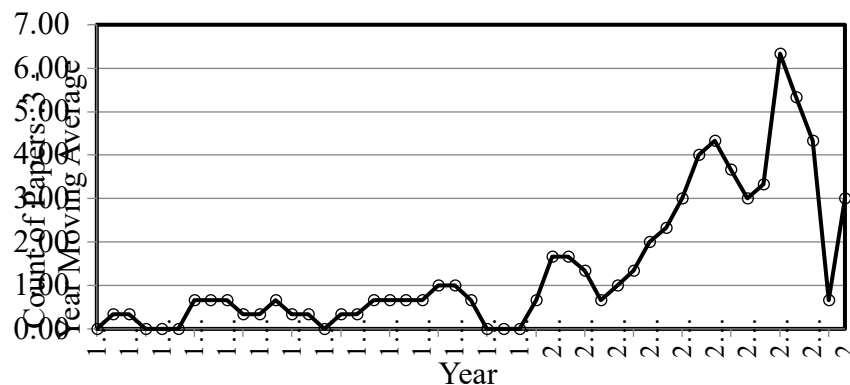


Figure A3: The trend for the number of papers published in all journals with a three-year moving

average.

The count of papers by disease type is listed in Table A1. Papers that did not focus on any specific disease have been grouped under the general category. Disease-related research invariably gains momentum after the disease outbreak and due to the severity of the outbreak. The analysis techniques found include: simulation, mathematical programming, stochastic modeling, statistical analysis, system analysis, game theory, decision analysis, bayesian method, machine learning, graph/network theory and heuristics. Some papers developed Decisions Support Systems (DSS). The type of data used include; field & archival (F&A), hypothetical, and real. Some papers present case studies; and some use no data. Cross tabulations of this information are included in the following five tables: Table A2: Disease vs. Analysis Technique, Table A3: Disease vs. Type of Data, Table A4: Analysis Technique vs. Type of Data, and Table A5: Category vs. Type of Data, and Table A6: Category vs Analysis Technique.

Table A1: Count of research papers by disease type by year.

Diseases	1972	1978	1981	1983	1987	1989	1990	1992	1993	1999	2000	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2018	2019	TOTAL
General <sup>1</sup>	1	2	1		1			1						1					2			2		4		1	2	1	18
HIV/AIDS						1	1		1	2	2	1	1		1	1	1	1	1	1				1					16
Influenza															1		1	2	2	1		1	2	4					14
Swine flu (H1N1)				1																		1	1	1				1	5
Anthrax																1			1									1	3
Ebola																										3		3	
H5N1 flu																					1		1				1	3	
Hepatitis C											1							1										1	3
Cholera																											1	1	2
Foot-and-mouth disease (FMD)																			1					1					2
Smallpox															2														2
Tuberculosis																		1		1									2
Cutaneous leishmaniasis																										1		1	
Measles																				1									1
Meningitis <sup>2</sup>																					1								1
Plague									1																				1
Respiratory, diarrhoea, and abdominal pain <sup>2</sup>																				1									1
Ross River																				1									1
SARS																									1				1
TOTAL	1	2	1	1	1	1	1	1	2	2	3	1	1	1	2	4	2	5	7	6	2	4	4	11	1	1	8	5	80

<sup>1</sup> A general paper does not consider any specific disease(s).

<sup>2</sup> These diseases can be either viral or bacterial.

<sup>3</sup> Note: COVID-19 is not included in this table since the disease started in 2020.

<sup>4</sup> Note: The total number of papers in Table A1 is 80 because some papers have studied more than one disease.

Table A2: Count of papers for disease type versus analytical technique.

Diseases vs. Analysis Technique	Simulation	Mathematical Programming	Stochastic Modelling	Statistical Analysis	DSS	System Analysis	Game Theory	Decision Analysis	Bayesian Method	Machine Learning	Graph/Network Theory	Heuristics	TOTAL
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HIV/AIDS	8	2	7	1	4	5							27
General	4	8	6	2	1		1	1	1	1	1		26
Influenza	3	4	4	2	1		2					1	17
Swine flu (H1N1)	2	1		1				2					6
H5N1 flu	2	2				1							5
Smallpox	1	1	1		1								4
Anthrax	1	1			1								3
Ebola		2				1							3
Foot-and-mouth disease (FMD)			1	1					1	1			4
Hepatitis C	3												3
Tuberculosis	2		1										3
Cholera		2											2
Meningitis	1	1											2
Cutaneous leishmaniasis							1						1
Measles				1									1
Plague		1											1
Respiratory, diarrhoea, and abdominal pain				1									1
Ross River				1									1
SARS		1											1
TOTAL	27	26	20	10	8	7	4	3	2	2	1	1	111

Note: COVID-19 is not included in this table since the disease started in 2020.

Table A3: Count of papers for disease type versus type of data.

Diseases vs. Type of Data	F&A	Hypothetical	No Data	Real Data	Case Study	TOTAL
General	6	6	6	1		19
HIV/AIDS	12	1		3	1	17
Influenza	8	5	2			15
Swine flu (H1N1)	5					5
Ebola	3					3
H5N1 flu	2			1		3
Hepatitis C	3					3
Tuberculosis	2			1		3
Cholera	2					2
Cutaneous leishmaniasis	1			1		2
Foot-and-mouth disease (FMD)	1			1		2
Smallpox	2					2
Anthrax	1					1
Measles	1					1
Meningitis	1					1
Plague	1					1
Respiratory, diarrhoea, and abdominal pain	1					1
Ross River	1					1
SARS	1					1
TOTAL	54	12	8	8	1	83

Note: COVID-19 is not included in this table since the disease started in 2020.

Table A4: Count of papers by analysis technique vs. type of data.

Data Analysis vs. Type of Data	Simulation	Mathematical Programming	Stochastic Modelling	Statistical Analysis	DSS	System Analysis	Game Theory	Decision Analysis	Bayesian Method	Machine Learning	Graph/Network Theory	Heuristics
F&A	14	19	10	7	5	4	2	2	2		1	1
Hypothetical	6	2	3	1	1	1	1	1				
No Data	1	4	7				1			1		
Real Data	4			1	2	3	1		1	1	1	
Case Study	1		1		1							

Table A5: Percentage of papers by type of data in each category.

Category vs. Type of Data	F&A	Hypothetical	No Data	Real Data	Case Study
Warning Signals/Surveillance	57.14	14.29	-	28.57	-
Disease Propagation	66.67	13.33	13.33	6.67	-
Mitigation	58.82	17.65	23.53	-	-
New Product Development	50	25	25	-	-
Resource Management	85.71	14.29	-	-	-
Supply Chain Configuration	66.67	16.67	8.33	8.33	-
DSS for Managing Pandemics	58.33	16.67	-	16.67	8.33
Risk Assessment	66.67	-	-	33.33	-

Table A6: Percentage of papers by analysis technique method in each category.

Category vs. Analysis Technique	Simulation	Mathematical Programming	Stochastic Modelling	Statistical Analysis	DSS	System Analysis	Game Theory	Decision Analysis	Bayesian Method	Machine Learning	Graph/Network Theory	Heuristics
Warning Signals/Surveillance	-	10	-	50	-	-	-	10	10	10	10	-
Disease Propagation	5.26	36.84	42.11	-	-	10.53	-	-	-	5.26	-	-
Mitigation	33.33	23.81	38.10	-	-	-	-	4.76	-	-	-	-
New Product Development	60	-	20	20	-	-	-	-	-	-	-	-
Resource Management	75	25	-	-	-	-	-	-	-	-	-	-
Supply Chain Configuration	46.15	15.38	-	-	-	-	30.77	-	-	-	-	7.69
DSS for Managing Pandemics	4.35	30.43	8.70	4.35	30.43	13.04	-	4.35	4.35	-	-	-
Risk Assessment	20	20	-	20	-	40	-	-	-	-	-	-

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